REMARKS

Claims 2, 3, 5, 12, 14 to 22 and 42 are pending in this application. Claim 42 has been added and is supported throughout the specification, e.g., at page 2, line 21 to page 3, line 14, and page 17, lines 1 to 7. No new matter has been added to the present application.

Rejection Under 35 U.S.C. §103

Claim 22 was rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Choi et al., U.S. Patent No. 6,248,360 (hereinafter "the '360 patent"), in view of Watts et al., U.S. Patent 6,465,626.

Applicants respectfully traverse this rejection. The present application is a continuation--in-part of the '360 patent and claims priority to the '360 patent. The disclosure of the '360 patent teaches the general concept of generic absorption enhancers. Therefore, the claims of the present application are entitled to a priority date as of the filing date of the '360 patent. Therefore, the '360 patent is not prior art with respect to the present claims. Further, the '360 patent is used by the Office as the primary reference in this rejection. Without the primary reference, a *prima facie* case of obviousness cannot be made. Therefore, applicants respectfully submit that the present rejection cannot stand and request that the rejection be reconsidered and withdrawn.

Claims 2, 3, 5, 12, 14 to 19 and 22 were rejected as allegedly unpatentable over Scott et al., U.S. Patent 6,458,387, in view of Watts.

Applicants respectfully traverse this rejection. Scott describes sustained release microspheres which, according to Scott, have a smooth surface and a plurality of openings (see, e.g., the Abstract of Scott and column 3, lines 23 to 25). The microspheres disclosed by Scott include, amongst other things, a macromolecule and a crosslinking energy source, or complexing agent. At the column and line numbers (i.e., Table 4 and column 22, lines 1 to 8) referred to in the present Office Action, Scott describes a large, presumably non-exclusive, list of therapeutic agents that can be used as macromolecules. Specifically, at Table 4, Scott lists at least 32

categories of therapeutic agents that can be used, one of which is "antibiotics and other antiinfective agents." In addition, Table I of Scott discloses another, larger list of agents that can be used as a macromolecule. This list includes about 47 different agents. Further, at columns 22 to 23 of Scott, over 200 different agents that can be used as a therapeutic agent are listed. One of the over 200 agents listed is cephalosporins, which generally includes at least first, second and third generation derivatives of cephalosporin C. Furthermore, Scott expressly discloses a preference for proteins and DNA as the macromolecule (see column 3, lines 28 to 29). With regard to a stabilizing mechanism for the microspheres, Scott discloses a variety of different crosslinking, complexing and energy sources that can be used (see, e.g., Table 3 of Scott). This includes about 28 different types of complexing agents, one of which is divalent cations.

The claims, on the other hand, are directed to a composition that includes, among other things, a specific class of cephalosporins, namely a third generation cephalosporin, and a divalent metal cation.

Applicants respectfully submit that Scott does not render the present invention obvious because, *inter alia*, Scott and its large lists of therapeutic agents does not teach or suggest applicants' invention. As discussed above, Scott discloses about 300 different classes and types of therapeutic agents. Nothing in the teachings of Scott suggest choosing an antibiotic from the long list of therapeutic agents or choosing cephalosporin from the list of antibiotics.

Moreover, Scott discloses numerous agents that can be used to stabilize the disclosed microcapsule including various energy sources and complexing agents. Nothing in Scott teaches or suggests selecting a divalent metal cation over all of the other complexing agents to combine with a cephalosporin over all of the other therapeutic agents. Applicants submit that no skilled practitioner, after reading Scott alone or in combination with Watts, would have chosen cephalosporins from among all of the therapeutic agents recited in Scott in combination with a divalent metal cation from all of the complexing agents to arrive at the present invention.

Applicants respectfully direct the Examiner's attention to §2144.08 (II) of the MPEP, which provides criteria for determining whether a skilled artisan would have been motivated to select a claimed species, including the size of the genus disclosed (§2144.08 (II)(A)(4)(a)).

Specifically, Section §2144.08 (II)(A)(4)(a) provides that "some motivation to select the claimed species...must be taught by the prior art." Section 2144.08.4(a) cites In re Baird, 16 F.3d 380 (Fed. Cir. 1994) and In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995), wherein the Federal Circuit held, respectively, that "[t]he fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious," and "no particular one of these [the disclosed genus] can be obvious unless there is something in the prior art to lead to the particular [species] and indicate that it should be prepared." Similarly, as discussed above, nothing in Scott would lead a skilled artisan to the claimed composition.

The Office further cites Watts, but Watts does nothing to remedy the defects of Scott. Watts describes, *inter alia*, drug compositions comprising chitosan, type A cationic gelatin, and a therapeutic agent. Watts also mentions absorption enhancers. However, Watts does not describe, or even suggest, cephalosporins. In addition, Watts does not teach or suggest combining cephalosporins with a divalent metal cation. Watts, like Scott, fails disclose each and every limitation of the amended claims by itself, and fails to do so even when combined with Scott.

Thus, neither Scott nor Watts, alone or in combination, teach or suggest the amended claims. For the reasons above, applicants respectfully request that the present rejection be reconsidered and withdrawn.

Claims 2, 3, 14, 15 and 22 were rejected as allegedly unpatentable over Hirai et al., U.S. Patent No. 4,616,008, in view of Plate et al., U.S. Patent No. 6,004,583, and further in view of Watts. Applicants respectfully traverse this rejection for the reasons discussed below.

Hirai describes compositions that include lipid soluble cephalosporin compounds and a cyclodextrin (see, e.g., Harai at column 1, lines 5 to 8). "Lipid soluble cephalosporin compounds," according to Harai, appear to be compounds obtained by esterifying a carboxyl group of a cephalosporin with various substituents at the 4-position. Such compounds display increased lipophilicity (see Harai at column 1, lines 16 to 34), which has the drawback of decreasing solubility in water and poor absorbability (see, e.g., Harai at column 1, lines 34 to

44). Harai goes on to describe Harai's approach to the problem of poor absorbability of these compounds (at column 1, lines 45 to 55):

> The present inventors conducted intensive research in an attempt to increase the in vivo absorbability after oral administration of these lipid soluble cephalosporin compounds and quite unexpectedly found that a composition comprising a lipid soluble cephalosporin compound and a cyclodextrin can provide much increased in vivo absorbability of the lipid soluble cephalosporin compound from gastrointestinal tract to body, and the lipid soluble cephalosporin taken in the body is then deesterified into the non-ester form of the cephalosporin, which exerts excellent antibacterial activities.

Based on the above, applicants conclude that Harai is focused on increasing the absorbability of low water solubility compounds created from cephalosporins.

Plate describes therapeutic-containing compositions adapted for oral administration. According to Plate, those compositions include a water insoluble but water swellable polymer, chemically modified with an enzyme inhibitor containing a chemical functionality having an interactive affinity for target receptors located on the transport barrier walls of the digestive tract, and at least one therapeutic of low oral bioavailability (see Abstract of Plate). The disclosure of Watts was discussed above and in the present Office Action.

Applicants submit that the amended claims are not rendered obvious by this combination of references because the combination provides neither the requisite motivation to combine the references to arrive at the present invention nor a reasonable expectation of success upon doing so. The claims are directed to pharmaceutical compositions comprising cephalosporins. Neither Harai itself, nor the combination of Harai, Plate and Watts, would have motivated skilled practitioners to use Harai's compositions with cephalosporins. Harai was concerned with increasing the absorbability of low water solubility compounds created from cephalosporin (i.e., cephalsoporins esterified with various substituents at the 4-position) and not cephalosporins in unmodified form. The Office Action also cites Plate, but Plate does nothing to remedy the shortcomings of Harai. While Plate does recite certain cephalosporins, Plate's solution to the problem of low absorption was, *inter alia*, to provide in a composition a water swellable polymer

chemically modified with an enzyme inhibitor containing a chemical functionality having an interactive affinity for digestive tract wall target receptors. Skilled practitioners faced with the problem of low absorption of cephalosporins, then, would not have explored modifying Harai's compositions using Plate because Harai would not have appeared to offer the needed solution and Plate would have appeared to provide a solution completely unrelated to any subject matter disclosed in Harai. Based on the focus of Harai and the problems Harai sought to solve, skilled practitioners would have had no reasonable expectation of success in attaining applicants' compositions with increased absorption properties even if they had done so. Neither Watts, nor the knowledge of those of ordinary skill in the art at the time the present application was filed, would have remedied those deficiencies.

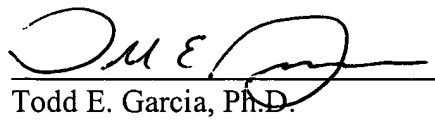
For the reasons discussed above, applicants respectfully submit that the amended claims are not rendered obvious by the Harai, Plate or Watts, alone or in combination. Thus, applicants request that the present rejection be reconsidered and withdrawn.

CONCLUSION

Enclosed is a $1,080 check for the Petition for Extension of Time fee for a five-month extension. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 19916-003001.

Respectfully submitted,

Date: 12/8/05



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